MMHCC
the Mouse Models of Human Cancers Consortium

MMHCC Newsletter September 2007

MouseLine

Mouse Genome Will Help Identify Causes of Environmental Disease

Research on the DNA of 15 mouse strains commonly used in biomedical studies is expected to help scientists determine the genes related to susceptibility to environmental disease. The body of data is now publicly available in a catalog of genetic variants, which displays the data as a mouse haplotype map, a tool that separates chromosomes in to many small segments, helping researchers find genes and genetic variations in mice that may affect health and disease. The haplotype map appearing online in the July 29th issue of *Nature* is the first published full descriptive analysis of the "Mouse Genome Resequencing and SNP Discovery Project" conducted by the National Institute of Environmental Health Sciences (NIEHS), part of the National Institutes of Health. "These data allow researchers to compare the genetic makeup of one mouse strain to another, and perform the necessary genetic analyses to determine why some individuals might be more susceptible to disease than another. This puts us one step closer to understanding individual susceptibility to environmental toxins in humans. We also hope that pharmaceutical companies developing new treatments for environmental diseases will find these data and this paper as a valuable resource," said David A. Schwartz. M.D., NIEHS Director.

The paper describes in detail the laborious and technology-driven approaches that were used to identify 8.27 million high quality SNPs distributed among the genomes of 15 mouse strains. Single Nucleotide Polymorphisms are single genetic changes or variations, that can occur in a DNA sequence.

Much of the project was conducted through a contract between the National Toxicology Program at NIEHS and Perlegen Sciences, Inc. of Mountain View Calif.

"The database of mouse genetic variation should facilitate a wide range of important biological studies, and helps demonstrate the utility of this array technology approach," said David R. Cox, M.D., Ph.D., chief scientific officer at Perlegen Sciences, Inc.

The Perlegen scientists used C57BL/6J the first mouse strain to undergo DNA sequencing as their standard reference to conduct the re-sequencing on the four wild-derived and eleven classical mouse strains. The technology used, the oligonucleotide array, was also used to discover common DNA variation in the human genome.

The arrays looked at about 1.49 billion bases (58 percent) of the 2.57 billion base pair of their standard reference strain. The data were then used to develop the haplotype map which contains 40,898 segments.

"The data will be a valuable resource to many, including the National Toxicology Program," Schwartz says. The National Toxicology Program (NTP) is an interagency program, headquartered at NIEHS, with the mission to coordinate, conduct and communicate toxicological research across the U.S. government.

MouseLine cont.

"The NTP is looking forward to exploring the responses of these strains of mice to various environmental agents," said John Bucher, Ph.D., the new associate director of the NTP.

Frank M. Johnson, Ph. D., an NTP research geneticist and one of the authors of the Nature paper, adds that systematically characterizing even more mouse strains for susceptibility to toxins will not only help with genetic analysis, but better position researchers to do intervention studies.

The data are publicly available on the National Center for Biotechnology Information Web site at http://www.ncbi.nlm.nih.gov/SNP/ and at a Web site developed by Perlegen at http://mouse.perlegen.com which allows researchers to download SNPs, genotypes, and LR-PCR primer pairs, which are currently mapped to NCBI Build 36.

In addition to the NTP and Perlegen Sciences scientists, other key collaborators on the project include researchers from the Department of Computer Science and Department of Human Genetics, University of California, Los Angeles; the Department of Computer Science and Engineering, University of California, San Diego; The Jackson Laboratory, Bar Harbor, Maine; Broad Institute of Harvard and MIT; and the Center for Human Genetic Research, Massachusetts General Hospital.

The National Institute of Environmental Health Sciences (NIEHS), a component of the National Institutes of Health, supports research to understand the effects of the environment on human health. For more information on environmental health topics, please visit our website at http://www.niehs.nih.gov/.

The National Institutes of Health (NIH) — *The Nation's Medical Research Agency* — includes 27 Institutes and Centers and is a component of the U.S. Department of Health and Human Services. It is the primary federal agency for conducting and supporting basic, clinical and translational medical research, and it investigates the causes, treatments, and cures for both common and rare diseases. For more information about NIH and its programs, visit http://www.nih.gov .

Reference: Kelly A. Frazer, Eleazar Eskin, Hyun Min Kang, Molly A. Bogue, David A. Hinds, Erica J. Beilharz, Robert V. Gupta, Julie Montgomery, Matt M. Morenzoni, Geoffrey B. Nilsen, Charit L. Pethiyagoda, Laura L. Stuve, Frank M. Johnson, Mark J. Daly, Claire M. Wade, David R. Cox. A sequence-based variation map of 8.27 million SNPs in inbred mouse strains. *Nature*, 2007.

Source: NIH Press Release
http://www.nih.gov/news/pr/jul2007/niehs-29.htm

Meetings

September 9 – 13, 2007
Phenotyping Mouse Models of Human Lung Disease
(Formerly Titled: "Workshop on Modeling Pulmonary Function in Mice")
Bar Harbor, Maine
Meeting Information: http://www.jax.org/courses/events/coursedetails.do?id=432&detail=scope

September 17 – 20, 2007
AACR-Second Annual Conference on Molecular Diagnostics in Cancer Therapeutic Development: Maximizing Opportunities for Personalized Treatment
Atlanta, Georgia
Meeting Information: http://www.aacr.org/home/scientists/meetings--workshops/molecular-diagnostics-in-cancer-therapeutic-development.aspx

September 18, 2007
Workshop on How to Thaw and Surgically Transfer Mouse Embryos
LaJolla, California
Meeting Information: http://www.jax.org/courses/events/coursedetails.do?id=573&detail=regproc

September 19 – 21, 2007
RNAi Europe
Barcelona, Spain
Meeting Information: http://www.selectbiosciences.com/conferences/rnaieurope07/

September 24 - 25, 2007
Fundamentals & Practical Aspects of Imaging in Clinical Trials
San Francisco, California
Meeting Information: http://www.iirusa.com/imaging/27347.xml

September 30 – October 6, 2007
6th Annual Workshop on the Pathology of Mouse Models for Human Disease
Bar Harbor, Maine
Meeting Information: http://www.jax.org/courses/events/coursedetails.do?id=450&detail=scope

October 10 – 13, 2007
The 2007 International Conference on Glioma Research and Therapy
Boston, Massachusetts
Meeting Information: http://www.glioma2007.org/

Meetings cont.

October 11 – 17, 2007
Short Course on Complex Trait Analysis
Bar Harbor, Maine
Meeting Information: http://www.jax.org/courses/events/coursedetails.do?id=449&detail=scope

October 15 – 17, 2007
Quantitative PCR, Microarrays, and Biological Validation: Capturing the Complete Biological Story
Providence, Rhode Island
Meeting Information: http://www.healthtech.com/2007/qpe/index.asp

October 17 - 20, 2007
AACR-Advances in Breast Cancer Research: Genetics, Biology and Clinical Applications
San Diego, California
Meeting Information: http://www.aacr.org/home/scientists/meetings--workshops/special-conferences/advances-in-breast-cancer-research.aspx

Notices and Funding Opportunities

Announcing the NIA Mutant Mouse Aging Colony for Biogerontology Research
NOT-AG-07-007
National Institute on Aging
http://grants.nih.gov/grants/guide/notice-files/NOT-AG-07-007.html

Request for Information. Agents to be tested for Preclinical Efficacy in Prevention or Reversal of Diabetic Complications in Rodent Models.
NOT-DK-07-013
National Institute of Diabetes and Digestive and Kidney Diseases
http://grants.nih.gov/grants/guide/notice-files/NOT-DK-07-013.html

Nutrition and Alcohol-Related Health Outcomes (R01, R03, R21)
PA-07-403, PA-07-404, PA-07-405
National Institute on Alcohol Abuse and Alcoholism
National Cancer Institute
Office of Dietary Supplements
http://grants.nih.gov/grants/guide/pa-files/PA-07-403.html
http://grants.nih.gov/grants/guide/pa-files/PA-07-404.html
http://grants.nih.gov/grants/guide/pa-files/PA-07-405.html

Lymphatic Biology in Health and Disease (R01)
PAR-07-420
National Heart, Lung, and Blood Institute
National Institute of Child Health and Human Development
National Institute of Diabetes and Digestive and Kidney Diseases
National Institute of Nursing Research
http://grants.nih.gov/grants/guide/pa-files/PAR-07-420.html

Data Ontologies for Biomedical Research (R01)
PAR-07-425
Multiple Institutes
http://grants.nih.gov/grants/guide/pa-files/PAR-07-425.html

Sharing Data and Tools: Federation using the BIRN and caBIG Infrastructures (R01)
PAR-07-426
Multiple Institutes
http://grants.nih.gov/grants/guide/pa-files/PAR-07-426.html

caBIG™ Tools

Intended for: Biologists, bioinformatics analysts and others with high throughput genomic data
Area of focus: Genome Annotation
Architecture Type: Desktop Application, Web Application - Remote application with data uploads/downloads through web interface

GoMiner™ is a tool for biological interpretation of 'omic' data – including data from gene expression microarrays. Omic experiments often generate lists of dozens or hundreds of genes that differ in expression between samples, raising the question “What does it all mean biologically?” To answer this question, GoMiner leverages the Gene Ontology (GO) to identify the biological processes, functions and components represented in these lists. Instead of analyzing microarray results with a gene-by-gene approach, GoMiner classifies the genes into biologically coherent categories and assesses these categories.

The application can be found at: http://discover.nci.nih.gov/gominer/start.jsp

For more information visit: https://cabig.nci.nih.gov/tools/GOMiner